UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/866,033	05/25/2001	Ellen R. Bolte	6917 P 002	4271

7590 07/31/2003

Jordan newmark, Esq.
RUDEN, McCLOSKY, SMITH, SCHUSTER & RUSSELL, P.A.
200 EAST BROWARD DOULEVARD
SUITE 1500
FORT LAUDERDALE, FL 33301

EXAMINER	
KAM, CHIH MIN	
ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 07/31/2003

14

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/866,033	Applicant(s) BOLTE, ELLEN R.	
	Examiner Chih-Min Kam	Art Unit 1653	

-- The MAILING DATE of this communicati n appears on the cover sheet with the c rrespondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 June 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4-7 and 15-36* is/are pending in the application.

4a) Of the above claim(s) *15-36* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2 and 4-7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4)☐ Interview Summary (PTO-413) Paper No(s). _____ .
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other: .

DETAILED ACTION

Status of the Claims

1. Claims 1, 2, 4-7 and 15-36 are pending.

Applicants' amendment filed on June 3, 2003 (Paper No. 13) and the Declaration of Inventor, Ellen Bolte filed under 37 C.F.R. 1.131 on May 5, 2003 are acknowledged. Applicants' response and the Declaration of Ellen Bolte have been fully considered. Claims 1, 2 and 4-7 have been amended, claims 3 and 8-14 have been cancelled, and claims 15-36 are non-elected inventions, thus withdrawn from consideration. Therefore, claims 1, 2 and 4-7 are examined.

Rejection Withdrawn

Claim Rejections - 35 USC § 112

2. The previous rejection of claims 3 and 8-14, under 35 U.S.C.112, first paragraph, is withdrawn in view of applicants' cancellation of the claim and applicants' response at pages 4-5 in Paper No. 13.

3. The previous rejection of claims 1, 3-8, 10-14, under 35 U.S.C.112, second paragraph, regarding the terms "one mental disorder" and "an antimicrobial composition", is withdrawn in view of applicants' amendment to the claim, applicants' cancellation of the claim, and applicants' response at pages 5-6 in Paper No. 13.

Claim Rejections - 35 USC § 102

4. The previous rejection of claims 8-12 and 14 under 35 U.S.C. 102(b) as being anticipated by the Web site of UWHC Antimicrobial Use Guide, Eighth Edition, July 1995-June 1996, is

withdrawn in view of applicants' cancellation of the claim, and applicants' response at page 6 in Paper No. 13.

5. The previous rejection of claim 13 under 35 U.S.C. 102(b) as being anticipated by the Web site of INCHEM, is withdrawn in view of applicants' cancellation of the claim, and applicants' response at page 6 in Paper No. 13.

6. The previous rejection of claim 3 under 35 U.S.C. 102(a) as being anticipated by Sandler *et al.* (CID, 30, 213-214 (January 2000)), is withdrawn in view of applicants' cancellation of the claim in Paper No. 13.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claim 1, 2 and 4-7 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating an individual exhibiting symptoms of autistic disorder or atypical psychosis, the method comprises administering to the individual an antimicrobial composition containing metronidazole in an amount effective to inhibit or ameliorating the symptoms of the autistic or atypical disorder; and of treating an individual exhibiting symptoms of atypical psychosis, comprising administering to the individual an effective amount of metronidazole as indicated by the prior art, does not reasonably provide enablement a method for treating an individual exhibiting a pervasive developmental disorder, comprising administering to the individual an antimicrobial composition containing a nitroimidazole to inhibit or eliminate the pervasive developmental disorder, wherein the specific

pervasive developmental disorder and the specific nitroimidazole compound are not identified. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claims 1, 2 and 4-7 encompass a method for treating an individual exhibiting a pervasive developmental disorder, comprising administering to the individual an antimicrobial composition comprising a nitroimidazole or metronidazole to inhibit or eliminate the pervasive developmental disorder (claims 1, 2 and 4-7). The specification, however, only discloses cursory conclusions (pages 3-5) without data supporting the findings, which state that administration of broad-spectrum antimicrobials has a profound effect on the normal gastrointestinal flora and can result in colonization of antimicrobial-resistant organisms such as *Clostridium difficile*, which would produce neurotoxins that mediate neurological disruption, and the present invention provides an antibacterial therapy directed to inhibit or eliminate these proliferating species to improve mental function. There are no indicia that the present application enables the full scope in view of treating a pervasive developmental disorder using an antimicrobial composition comprising a nitroimidazole as discussed in the stated rejection. The present application provides no indicia and no teaching/guidance as to how the full scope of the claims is enabled. The factors considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F2d at 731,737, 8 USPQ2d at 1400,1404 (Fed. Cir.1988)). The factors most relevant to this rejection are the breath of the claims, the presence of working examples, the state of the prior art and relative skill of those in the art, the unpredictability of the art, the nature of

the art, the amount of direction or guidance presented, and the amount of experimentation necessary.

(1). The breath of the claims:

The breath of the claims is broad and encompasses unspecified variants regarding the pervasive developmental disorders to be treated and the nitroimidazoles contained in the antimicrobial compositions, which are not adequately described or demonstrated in the specification.

(2). The presence or absence of working examples:

The specification demonstrates the treatment of children with autistic disorder, atypical psychosis or attention deficit/hyperactivity using vancomycin, metronidazole or clarithromycin (Examples 1-7). There are no other working examples indicating the claimed methods in association with various pervasive developmental disorders using different nitroimidazoles.

(3). The state of the prior art and relative skill of those in the art:

The prior art (Sandler et al., CID 30, 213-214 (January 2000)) indicates administration of metronidazole to a child having atypical psychosis improves the psychiatric condition of the patient during the treatment, however, the general knowledge and level of the skill in the art do not supplement the omitted description, the specification needs to provide specific guidance on the treating conditions such as the dose and the time for various pervasive developmental disorders using a different nitroimidazole in the antimicrobial composition to be considered enabling for variants.

(4). The amount of direction or guidance presented and the quantity of experimentation necessary:

The claims are directed to a method for treating an individual exhibiting a pervasive developmental disorder, comprising administering to the individual an antimicrobial composition containing a nitroimidazole to inhibit or eliminate the pervasive developmental disorder. The specification indicates an antimicrobial, which has certain properties, is selected for antimicrobial therapy in treating mental disorders with a gut flora etiology (page 5, line 20-page 6, line 15) and further demonstrates the treatment of children with autistic disorder, atypical psychosis or attention deficit/hyperactivity using vancomycin, metronidazole or clarithromycin (Examples 1-7). However, the specification fails to provide the treating conditions such as the dose and the time for treating various pervasive developmental disorders using a different nitroimidazole, nor indicates the effect of the treatment. From the examples of treatment (Examples 1-7), it is not apparent how an individual with a different pervasive developmental disorder is treated using a different nitroimidazole, and what effects the antimicrobial composition containing a different nitroimidazole would produce. Moreover, there are no working examples indicating the use and the effect of a different nitroimidazole in treating a different pervasive developmental disorder. Since the specification fails to provide sufficient teachings on treating conditions such as the dose, the time for various pervasive developmental disorders using a different nitroimidazole, it is necessary to have additional guidance and to carry out further experimentation to assess the effects of various nitroimidazoles.

(5). Predictability or unpredictability of the art:

The claims are directed to a method for treating an individual exhibiting a pervasive developmental disorder by administering to the individual an antimicrobial composition containing a nitroimidazole. Since the treating conditions for various pervasive developmental

disorders using a different nitroimidazole are not sufficiently described, the outcome of the claimed method is highly unpredictable. For example, a case of metronidazole-induced psychotic disorder has been reported using a 5-day regimen of intravenous metronidazole (1 g/day) for treatment of adnexitis (Schreiber et al., Am. J. Psychiatry 154, 1170-1171 (1997)).

(6). Nature of the Invention

The scope of the claim includes treating a pervasive developmental disorder using an antimicrobial composition containing a nitroimidazloe, however the specification has not demonstrated the treatment of various pervasive developmental disorders using various nitroimidazoles. Thus, the disclosure is not enabling for reasons discussed above.

In summary, the scope of the claim is broad, while the working example does not demonstrate the claimed variants, and the teaching in the specification is limited, therefore, it is necessary to have additional guidance and to carry out further experimentation to assess the effects of various nitroimidazoles in treating pervasive developmental disorders.

In response, applicants indicate the claims have been amended in accordance with the portions of the specification deemed enabling by the Examiner, and the scope of the amended claims bears a reasonable correlation to the scope of enablement provided by the specification. The response have been fully considered, however, the argument is not found persuasive because the claim is directed to a method of treating an undefined pervasive developmental disorder using an undefined nitroimidazole, where the full scope of the claims is not enabled as indicated above.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 1, 2 and 4-7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 2 and 4-7 are indefinite because the claim lacks essential steps in the method of treating an individual exhibiting a pervasive developmental disorder. The omitted step is effective amount of the antimicribial composition used for the treatment. Claims 2 and 4-7 are included in the rejection because they are dependent on rejected claims and do not correct the deficiency of the claim from which they depend.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

9. Claims 1, 2, 4 and 5 are rejected under 35 U.S.C. 102(a) as anticipated by Sandler *et al.* (CID, 30, 213-214 (January 2000)).

Sandler *et al.* disclose a 14-year boy with Crohn's disease, who also developed atypical psychosis, was treated with metronidazole (250 mg t.i.d.), prednisone and mesalamine, within two weeks, both his GI and psychiatric symptoms dramatically abated (pages 213-214; claims 1, 2 and 4). Subsequent deterioration in behavior was first noted 2 months after metronidazole treatment was discontinued, and 3 months after the psychiatric relapse, a second 1 month course

of metronidazole (500 mg t.i.d. orally for 30 days) was initiated (page 214, claim 5). Within 3 weeks, a dramatic improvement in his psychiatric condition was noted, and by 5 weeks, he was essentially normal and not receiving any antipsychiatric medication.

In response, applicants indicate the inventor, Ellen Bolte is one of the authors of the publication of Sandler et al. (CID 30, 213-214, January 2000), and a declaration of Ellen Bolte filed under 37 C. F. R. 1.131, including supporting statements by Ellen Bolte and Richard H. Sandler is used to overcome the reference by Sandler et al. (pages 6-7 of the response). In the supporting statement of Ellen Bolte, the inventor indicates she is an author of the publication of Sandler et al. (January 2000), she first conceived of the idea for the invention of the present application in 1995 and approached Dr. Richard Sandler in 1996 to assist her in testing invention, and through case study and data analysis that began prior to and was the subject matter of the publication of Sandler et al. (January 2000); the inventor further asserts that her diligence is demonstrated by her filing of three provisional patent applications (60/209,712, 60/214,813, and 60/240,582) prior to the present application, and her continued research in the subject matter of present application from prior to the publication date of the cited reference to the filing date of the present application; Richard Sandler also declares the original idea and the invention in the present application are solely inventor's, he and Ellen Bolte are the authors of the publication of Sandler et al. (January 2000), and Ellen Bolte invented the invention prior to January 2000, the publication date of the article.

The declaration filed on May 5, 2003 under 37 CFR 1.131 has been considered but is ineffective to overcome the Sandler et al. reference. The evidence submitted is insufficient to establish diligence from a date prior to the date of reduction to practice of the Sandler et al.

reference to either a constructive reduction to practice or an actual reduction to practice because the applicant has not provided any factual data indicating case study and data analysis that began prior to the publication of the reference.

Conclusions

10. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (703) 308-9437. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, Ph. D. can be reached on (703) 308-2923. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-0294 for regular communications and (703) 308-4227 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Chih-Min Kam, Ph. D. CMK
Patent Examiner

***
July 30, 2003

Christopher S. F. Low
CHRISTOPHER S. F. LOW
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600